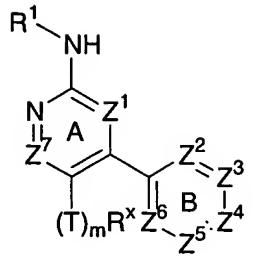
CLAIMS

1. A compound of formula **I**:



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is Q-Ar^1,

wherein Q is a C_{1-2} alkylidene chain wherein one methylene unit of Q is optionally replaced by O, NR, NRCO, NRCONR, $NRCO_2$, CO, CO_2, CONR, OC(O)NR, SO_2, SO_2NR, $NRSO_2$, $NRSO_2NR$, C(O)C(O), or $C(O)CH_2C(O)$;

Ar^1 is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar^1 is optionally substituted with q independent occurrences of Z-R^Z; wherein q is 0-5, Z is a bond or is a C_1-C_6 alkylidene chain wherein up to two non-adjacent methylene units of Z are optionally and independently replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR; and each occurrence of R^Z is independently selected from R', halogen, NO_2, CN, OR', SR', $N(R')_2$, NR'COR', $NR'CON(R')_2$, $NR'CO_2R'$, COR', CO_2R', OCOR', $CON(R')_2$, $OCON(R')_2$, SOR', SO_2R', $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, COCOR', or $COCH_2COR'$;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6}

aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Z^1 is N or CH;

Z^7 is N or $C(U)_nR^Y$;

T and U are each independently a bond or a saturated or unsaturated C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR;

m and n are each independently 0 or 1;

R^X and R^Y are each independently selected from R or Ar^1;

Z^2 is N or CR^2; Z^3 is N or CR^3; Z^4 is N or CR^4; Z^5 is N or CR^5; and Z^6 is N or CR^6, wherein each occurrence of R^2, R^3, R^4, R^5 or R^6 is independently R^U or $(V)_pR^V$, provided that a) no more than three of Z^2, Z^3, Z^4, Z^5 or Z^6 is N, and b) at least one of Z^3, Z^4 or Z^5 is CR^3, CR^4, or CR^5, respectively, and at least one of R^3, R^4, or R^5 is R^U,

each occurrence of R^U is $NRCOR^7$, $CONR(R^7)$, $SO_2NR(R^7)$, $NRSO_2R^7$, $NRCONR(R^7)$, $NRSO_2NR(R^7)$, or $CONRNR(R^7)$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, 1, or 2, Y is a bond or is O, S, NR^9, $-OCH_2-$, $-SCH_2$, $-NR^9CH_2$, $O(CH_2)_2-$, $-S(CH_2)_2$, or $-NR^9(CH_2)_2$, and R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form an optionally substituted 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each occurrence of V is a bond or a saturated or unsaturated C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR;

each occurrence of p is 0 or 1;

each occurrence of R^V is R or Ar^2; and

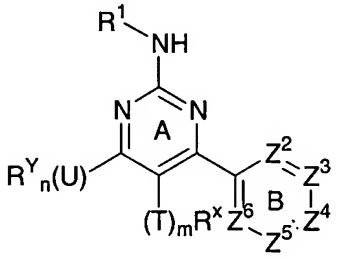
Ar^2 is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar^2 is optionally substituted with r independent occurrences of $W\text{-}R^W$; wherein r is 0-3, W is a bond or is a C_1-C_6 alkylidene chain wherein up to two non-adjacent methylene units of W are optionally replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR; and each occurrence of R^W is independently selected from R', halogen, NO_2, CN, OR', SR', $N(R')_2$, NR'COR', $NR'CON(R')_2$, $NR'CO_2R'$, COR', CO_2R', OCOR', $CON(R')_2$, $OCON(R')_2$, SOR', SO_2R', $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, COCOR', or $COCH_2COR'$;

provided that:

a) when Z^1 is N, Z^7 is CH; and ring B is phenyl and at least one of R^3 or R^4 is $NHCOR^7$, then R^1 is not phenyl only substituted with two or three occurrences of OR'; and

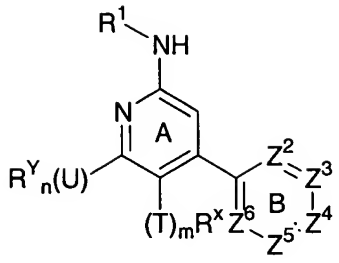
b) when Z^1 is N, Z^7 is CH; and ring B is phenyl and at least one of R^3 of R^4 is $NHCOR^7$, SO_2R^7, $CONRR^7$, then R^1 is not phenyl only substituted with one occurrence of $-CON(R')_2$ in the para position.

2. The compound according to claim 1, wherein Z^1 is N and the compound has the structure **II**:



II

3. The compound of claim 1, wherein Z^1 is CH and amino pyridines of general formula **III** are provided:



III

4. The compound of claim 1, wherein R^1 is an optionally substituted phenyl, cyclohexyl, cyclopentyl, pyridyl, morpholino, piperazinyl, or piperidinyl group

5. The compound of claim 1, wherein R^1 is an optionally substituted from phenyl, cyclohexyl, or pyridyl group.

6. The compound of claim 1, wherein R^1 is optionally substituted phenyl.

7. The compound of claim 1, wherein q is 0, 1, 2, or 3 and each independent occurrence of ZR^Z is C_{1-4}alkyl, $N(R')_2$, OR', SR', $CON(R')_2$, NR'COR', $NR'SO_2R'$, or $SO_2N(R')_2$.

8. The compound of claim 1, wherein q is 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$.

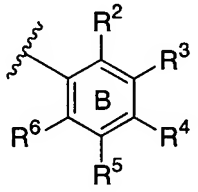
9. The compound of claim 1, wherein q is 1, and ZR^Z is in the meta position and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$.

10. The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are hydrogen, halogen, NO_2, CN, OR, SR or $N(R)_2$, or C_{1-4}aliphatic optionally substituted with oxo, OR, SR, $N(R)_2$, halogen, NO_2 or CN.

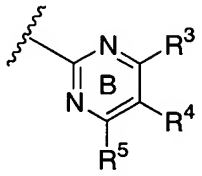
11. The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are each independently hydrogen, Me, OH, OMe or $N(R)_2$.

12. The compound of claim 1, wherein $(T)_mR^X$ and $(U)_nR^Y$ are each hydrogen.

13. The compound of claim 1, wherein ring B is one of rings **i-xiv:**



i



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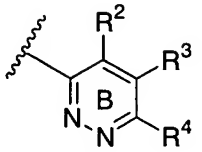
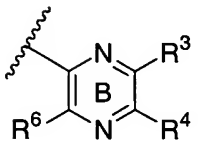
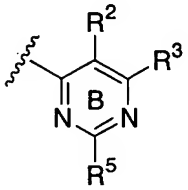


iii



iv



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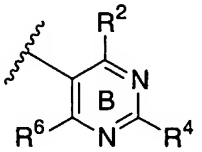
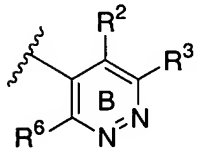
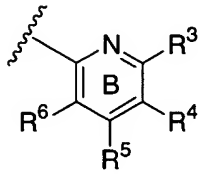


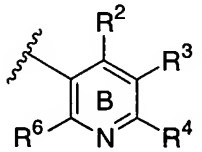
vi



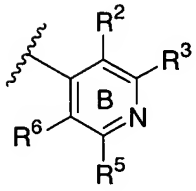
vii



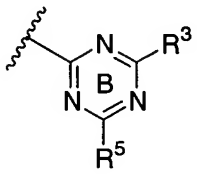
viii



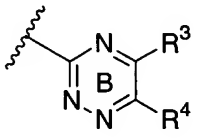
ix



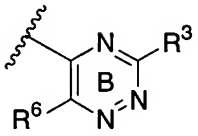
x



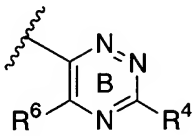
xi



xii



xiii



xiv

14. The compound of claim 1, wherein t is 0, Y is a bond, and R^8 is an optionally substituted aryl or heteroaryl moiety.

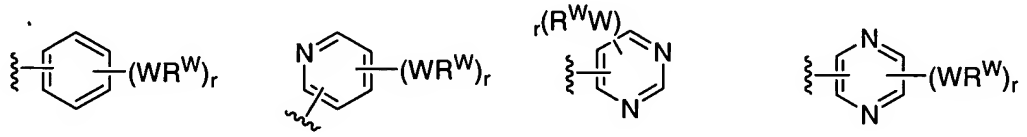
15. The compound of claim 1, wherein t is 0, Y is a bond, and R^8 is an optionally substituted heteroaryl moiety.

16. The compound of claim 1, wherein R^7 is $-CH_2-Y-R^8$, and Y is NR^9, O or S, and R^8 is an optionally substituted aryl or heteroaryl moiety.

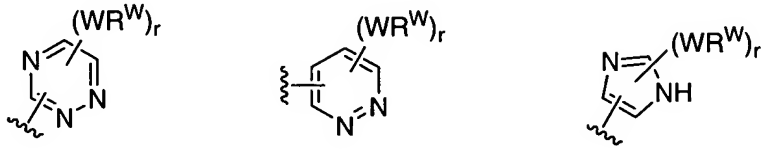
17. The compound of claim 1, wherein R^7 is $-CH_2-Y-R^8$, and Y is NR^9, O or S, and R^8 is an optionally substituted aryl moiety.

18. The compound of claim 1, wherein t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur.

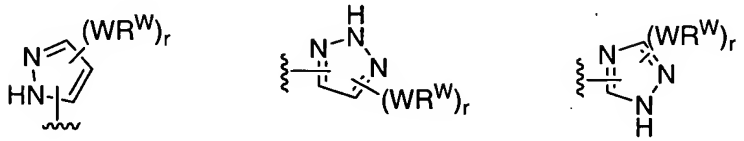
19. The compound of claim 1, wherein R^8 is a 5- or 6-membered aryl or heteroaryl group having one of the formulae:



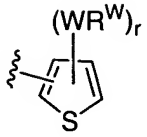
a **b** **c** **d**



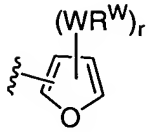
e **f** **g**



h **i** **j**



k



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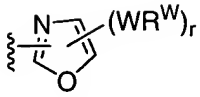
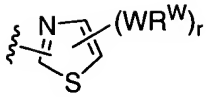


m



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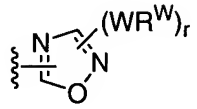
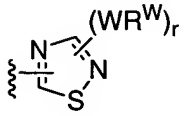
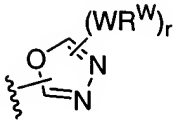


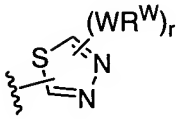
o



p

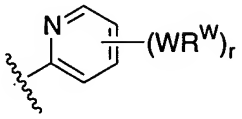


q

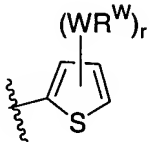


r

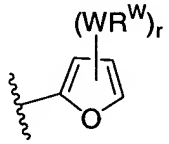
20. The compound of claim 1, wherein R^8 is a 5- or 6-membered heteroaryl group having one of the formulae:



b-i

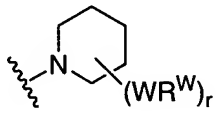


k-i

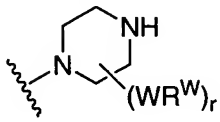


l-i

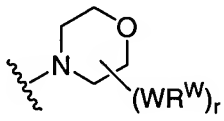
21. The compound of claim 1, wherein R^8 and R^9, taken together, form a group having one of the formulae:



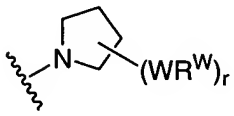
s



t



u



v

22. The compound of claim 1, wherein r is 0 or 1.

23. The compound of claim 19, 20, or 21, wherein r is 1, 2, or 3, and each occurrence of halogen, $C_{1\text{-}4}$alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR.

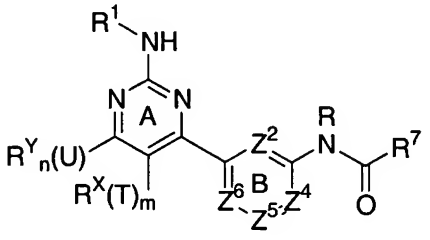
24. The compound of claim 19, 20, or 21, wherein t is 0, Y is a bond, and R^8 is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**.

25. The compound of claim 24, wherein R^8 is an optionally substituted heteroaryl group **b-i**, **k-i**, or **l-i**.

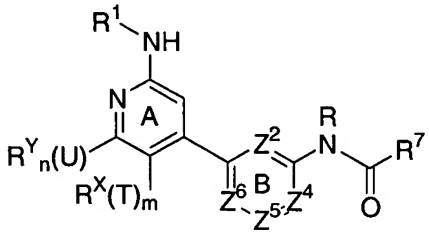
26. The compound of claim 1, wherein t is 1, Y is O, S or NR^9, and R^8 is optionally substituted phenyl.

27. The compound of claim 1, wherein t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together form an optionally substituted group selected from **s**, **u** or **v**.

28. The compound of claim 1, wherein Z^3 or Z^5 is CR^3 or CR^5, respectively, and R^3 or R^5 is $NRC(O)R^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, -OCH_2-, -SCH_2, -NR^9CH_2, $O(CH_2)_2$-, -$S(CH_2)_2$, or –$NR^9(CH_2)_2$, and wherein R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have the formula **II-A** or **III-A:**

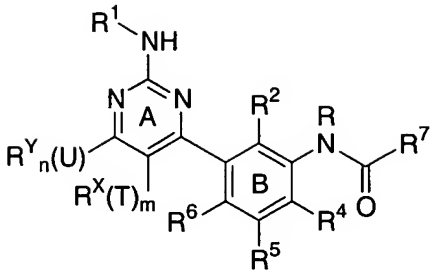


II-A

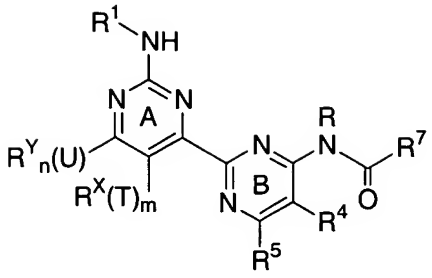


III-A

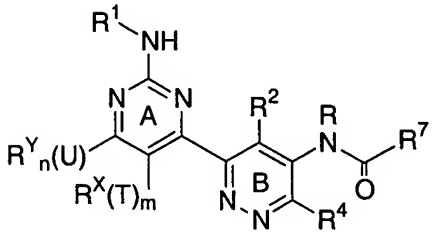
29. The compound of claim 28, wherein for compounds of formula **II-A** ring B is selected from **i, ii, iii, iv, v, vii, viii, ix, x, xi, xii,** or **xiii** and compounds have one of formulas **II-A-i, II-A-ii, II-A-iii, II-A-iv, II-A-v, II-A-vii, II-A-viii, II-A-ix, II-A-x, II-A-xi, II-A-xii,** or **II-A-xiii**:



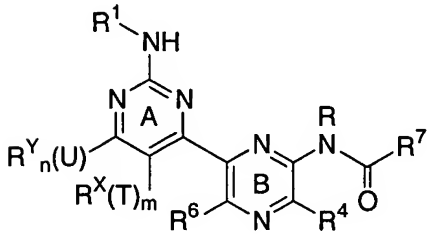
II-A-i



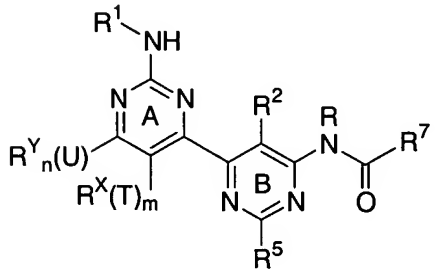
II-A-ii



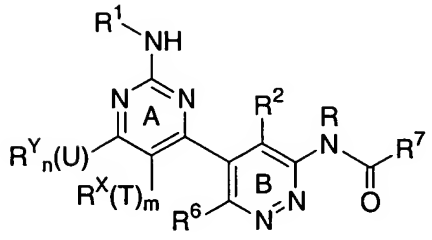
II-A-iii



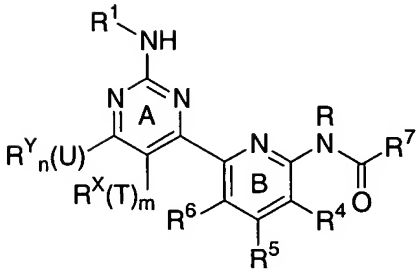
II-A-iv



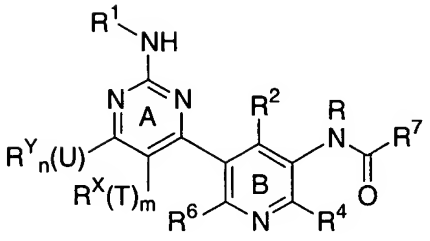
II-A-v



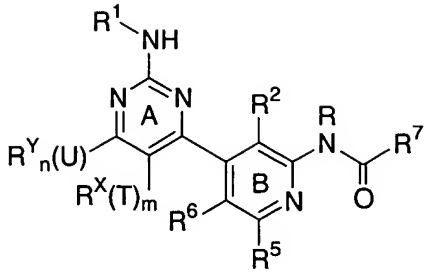
II-A-vii



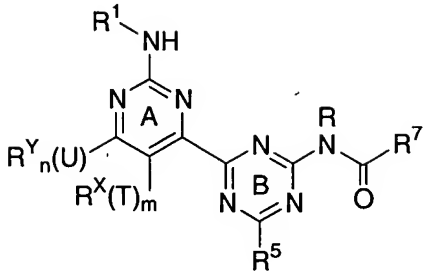
II-A-viii



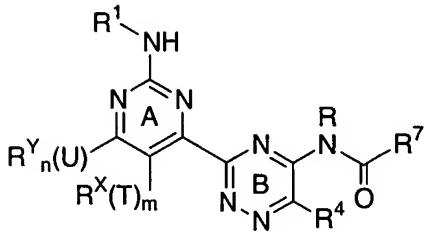
II-A-ix



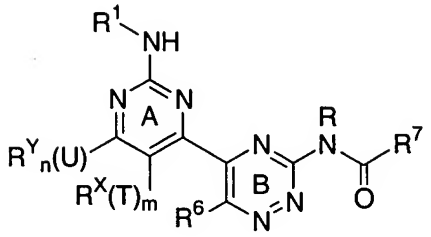
II-A-x



II-A-xi

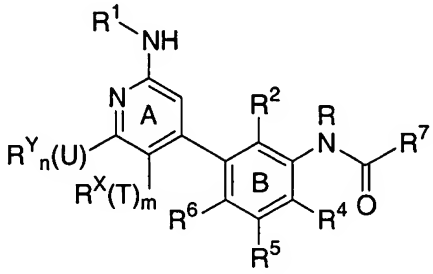


II-A-xii

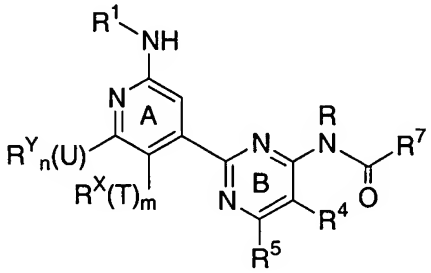


II-A-xiii

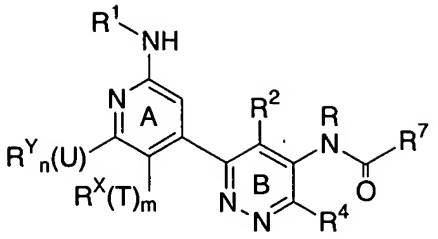
30. The compound of claim 28, wherein for compounds of formula **III-A** ring B is selected from one of **i, ii, iii, iv, v, vii, viii, ix, x, xi, xii,** or **xiii** and compounds have one of formulas **III-A-i, III-A-ii, III-A-iii, III-A-iv, III-A-v, III-A-vii, III-A-viii, III-A-ix, III-A-x, III-A-xi, III-A-xii,** or **III-A-xiii**:



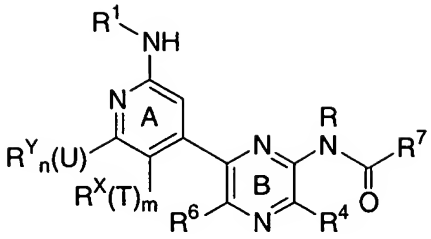
III-A-i



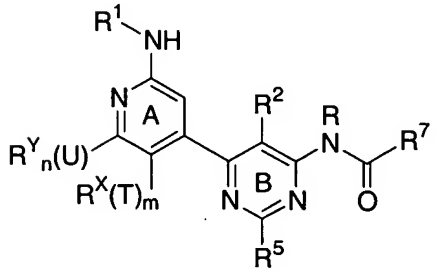
III-A-ii



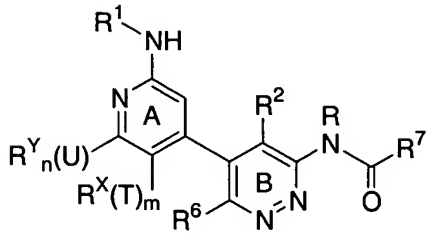
III-A-iii



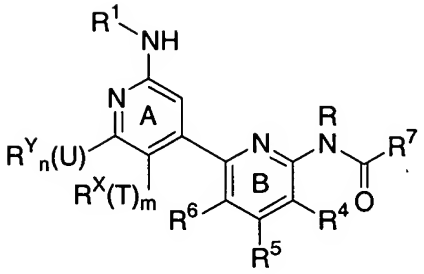
III-A-iv



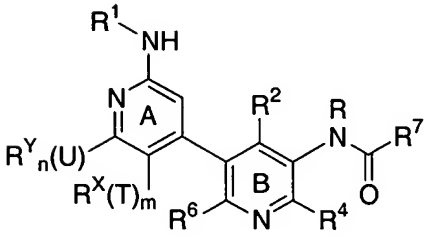
III-A-v



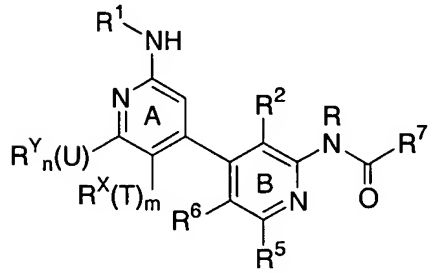
III-A-vii



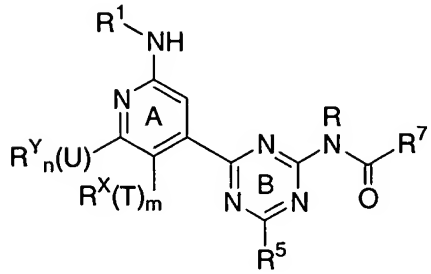
III-A-viii



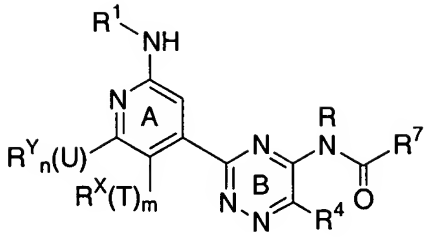
III-A-ix



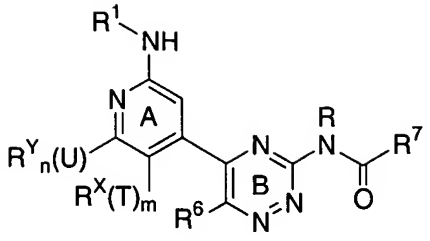
III-A-x



III-A-xi

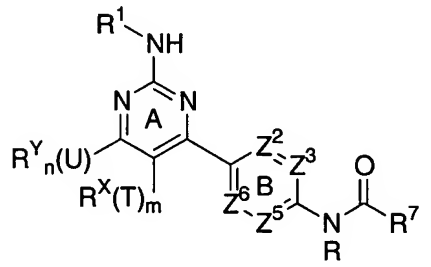


III-A-xii

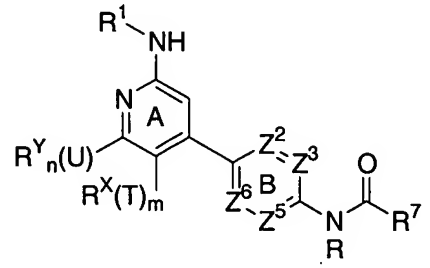


III-A-xiii

31. The compound of claim 1, wherein Z^4 is CR^4, and R^4 is $NRC(O)R^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, $-OCH_2-$, $-SCH_2$, $-NR^9CH_2$, $O(CH_2)_2-$, $-S(CH_2)_2$, or $-NR^9(CH_2)_2$, and wherein R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur, and compounds have one of formulas **II-B** or **III-B**:

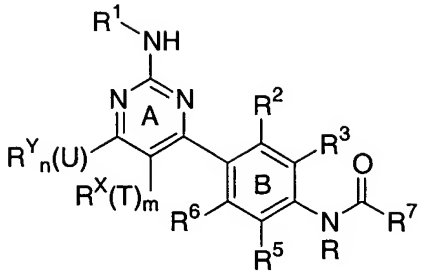


II-B

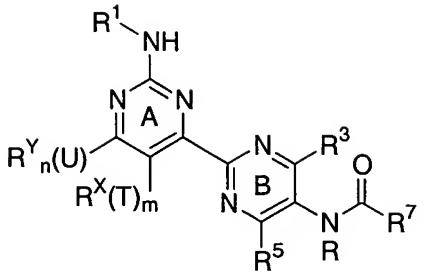


III-B

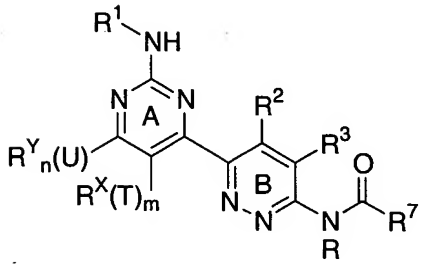
32. The compound of claim 31, wherein for compounds of formula **II-B,** ring B is selected from **i, ii, iii, iv, vi, viii, ix, xii,** or **xiv** and compounds have one of formulas **II-B-i, II-B-ii, II-B-iii, II-B-iv, II-B-vi, II-B-viii, II-B-ix, II-B-xii,** or **II-B-xiv**:



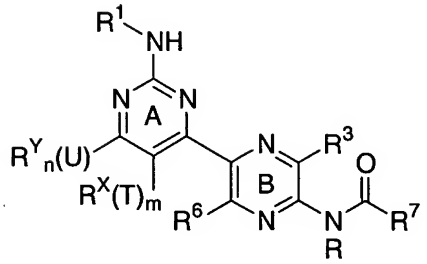
II-B-i



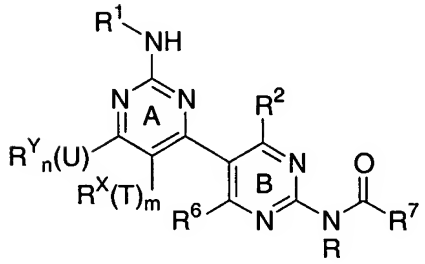
II-B-ii



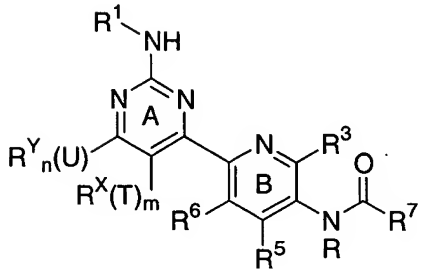
II-B-iii



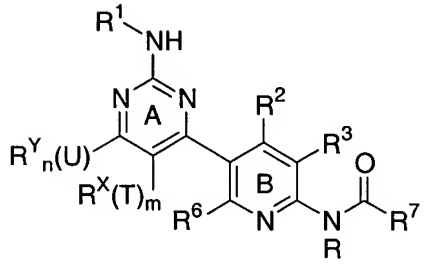
II-B-iv



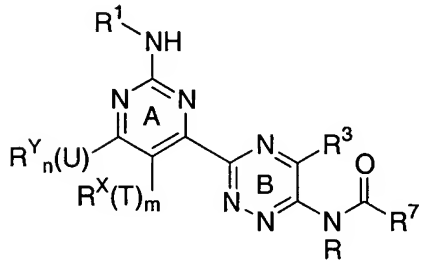
II-B-vi



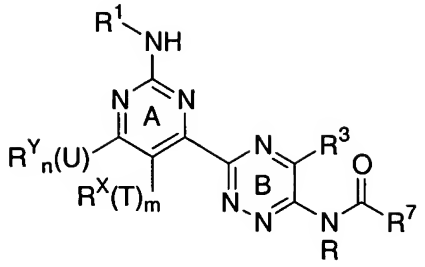
II-B-viii



II-B-ix

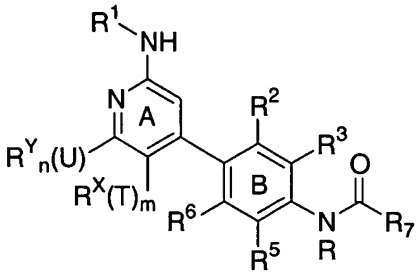


II-B-xii

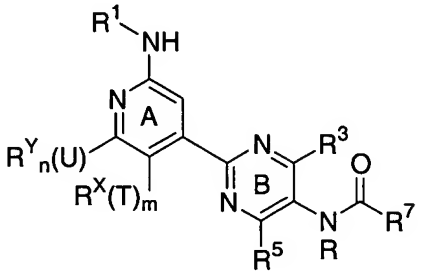


II-B-xiv

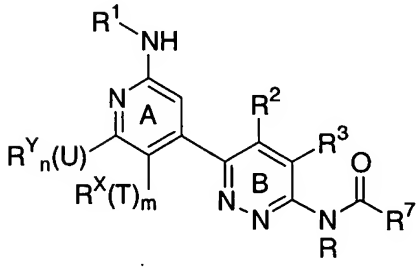
33. The compound of claim 31, wherein for compounds of formula **III-B,** ring B is selected from **i, ii, iii, iv, vi, viii, ix, xii,** or **xiv** and compounds have one of formulas **III-B-i, III-B-ii, III-B-iii, III-B-iv, III-B-vi, III-B-viii, III-B-ix, III-B-xii,** or **III-B-xiv**:



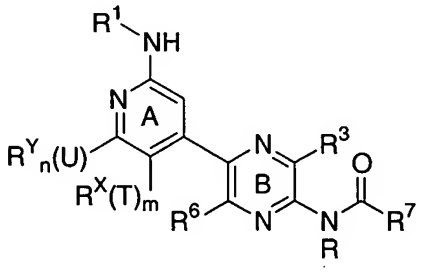
III-B-i



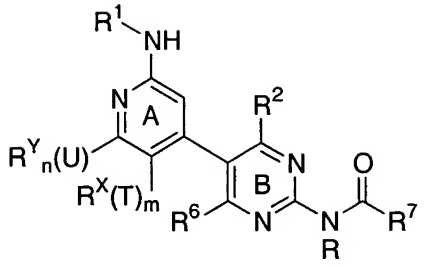
III-B-ii



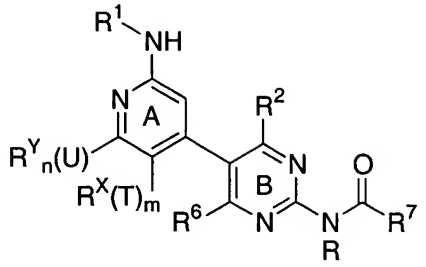
III-B-iii



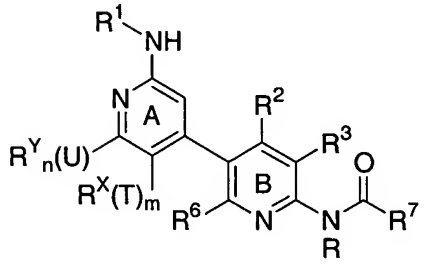
III-B-iv



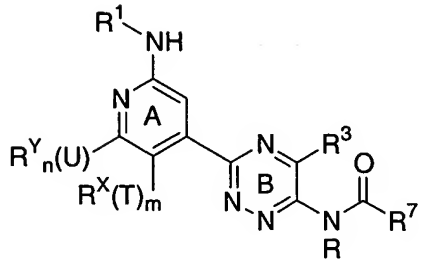
III-B-vi



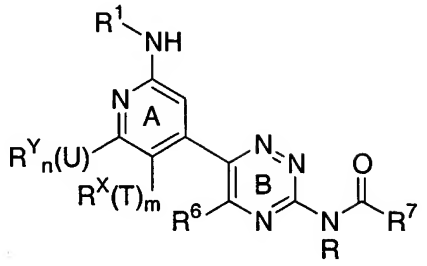
III-B-viii



III-B-ix

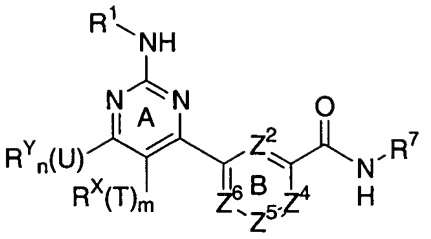


III-B-xii

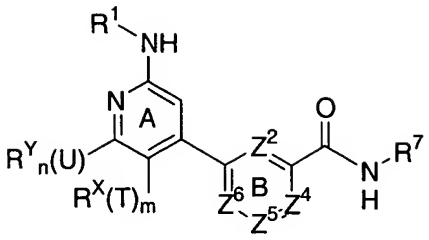


III-B-xiv

34. The compound of claim 1, wherein Z^3 or Z^5 is CR^3 or CR^5, respectively, and R^3 or R^5 is $C(O)N(R)(R^7)$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, $-OCH_2-$, $-SCH_2$, $-NR^9CH_2$, $O(CH_2)_2-$, $-S(CH_2)_2$, or $-NR^9(CH_2)_2$, and wherein R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have one of formulas **II-C** or **III-C:**

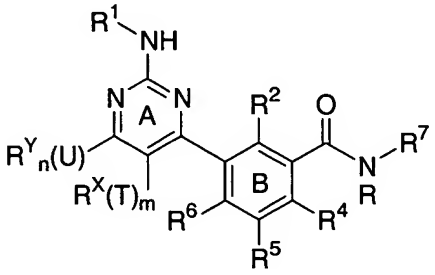


II-C

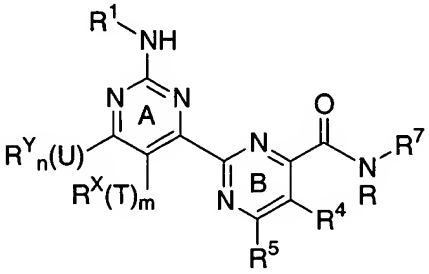


III-C

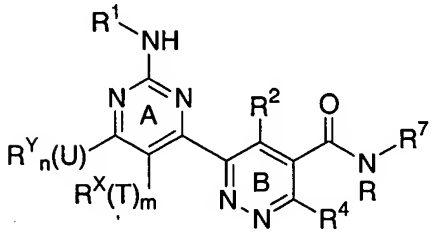
35. The compound of claim 34, wherein for compounds of formula **II-C**, ring B is selected from **i, ii, iii, iv, v, vii, viii, ix, x, xi, xii,** or **xiii** and compounds have one of formulas **II-C-i, II-C-ii, II-C-iii, II-C-iv, II-C-v, II-C-vii, II-C-viii, II-C-ix, II-C-x, II-C-xi, II-C-xii,** or **II-C-xiii**:



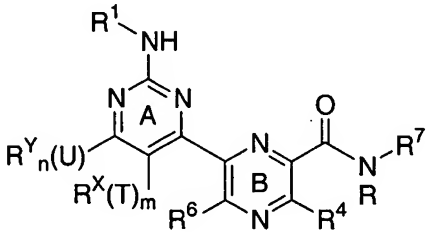
II-C-i



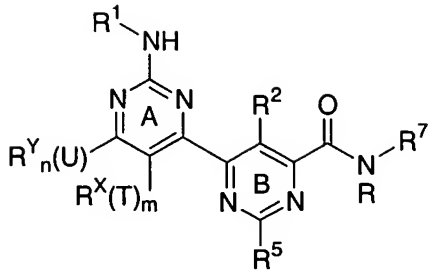
II-C-ii



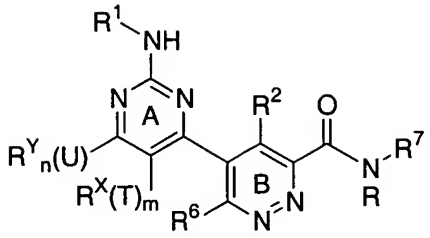
II-C-iii



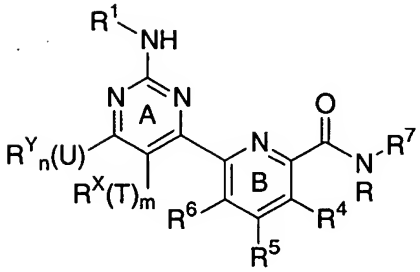
II-C-iv



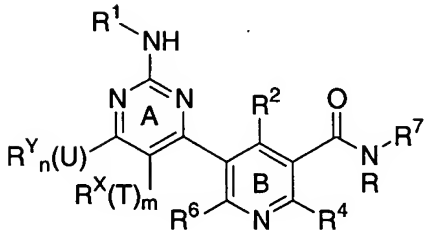
II-C-v



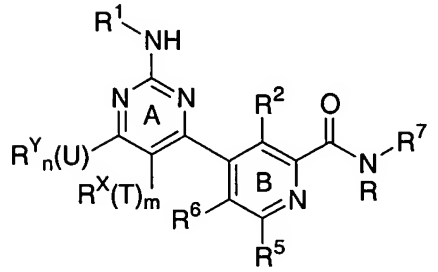
II-C-vii



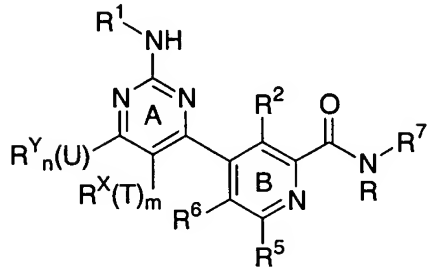
II-C-viii



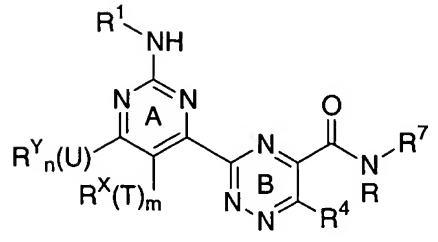
II-C-ix



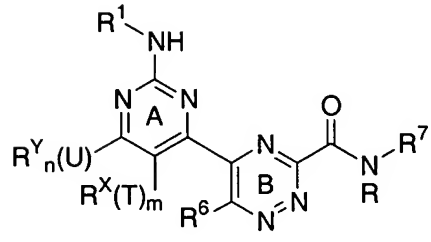
II-C-x



II-C-xi

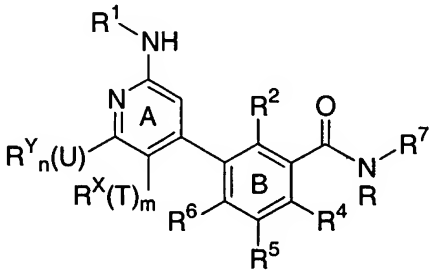


II-C-xii

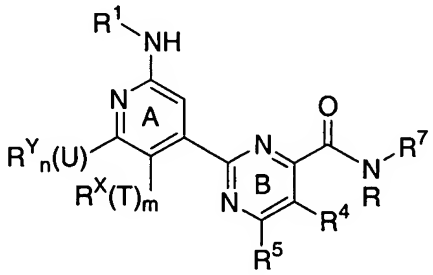


II-C-xiii

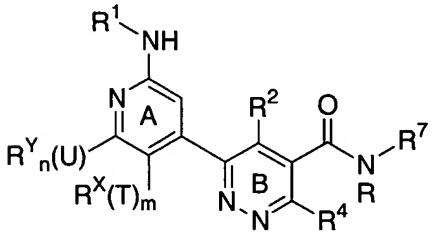
36. The compound of claim 34, wherein for compounds of formula **III-C,** ring B is selected from **i, ii, iii, iv, v, vii, viii, ix, x, xi, xii,** or **xiii** and compounds have one of formulas **III-C-i, III-C-ii, III-C-iii, III-C-iv, III-C-v, III-C-vii, III-C-viii, III-C-ix, III-C-x, III-C-xi, III-C-xii,** or **III-C-xiii** are provided as depicted below:



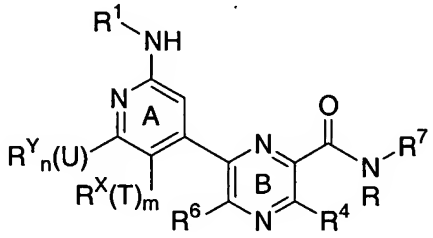
III-C-i



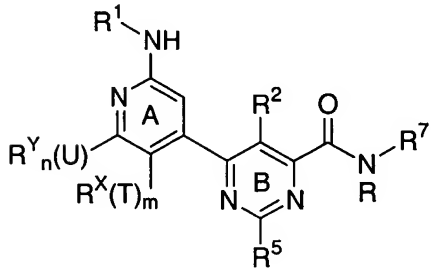
III-C-ii



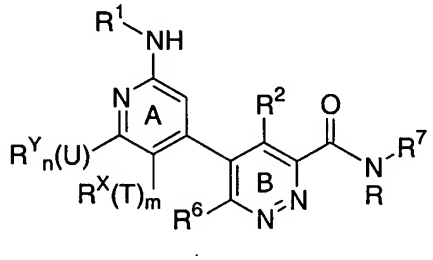
III-C-iii



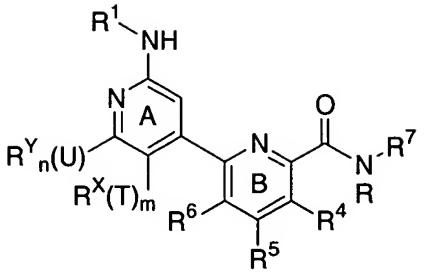
III-C-iv



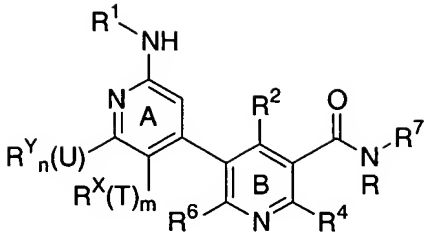
III-C-v



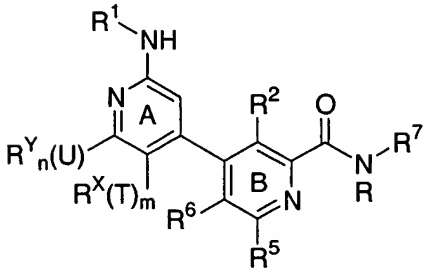
III-C-vii



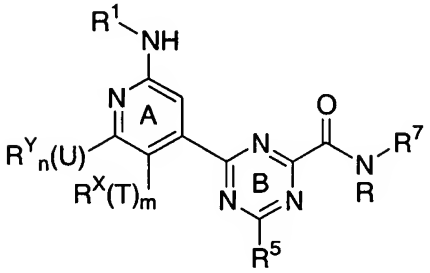
III-C-viii



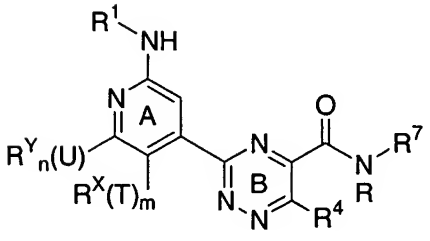
III-C-ix



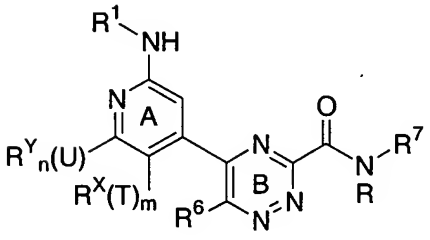
III-C-x



III-C-xi

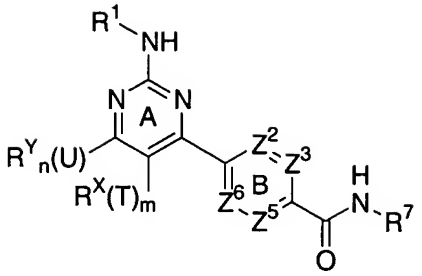


III-C-xii

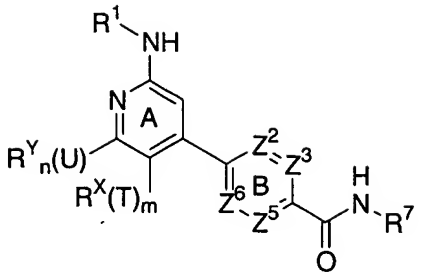


III-C-xiii

37. The compound of claim 1, wherein Z^4 is CR^4, and R^4 is $C(O)N(R)(R^7)$, wherein R^7 is $(CH_2)_t$-Y-R^8, wherein t is 0, 1 or 2, wherein Y is a bond or is O, S, NR^9, $-OCH_2-$, $-SCH_2$, $-NR^9CH_2$, $O(CH_2)_2-$, $-S(CH_2)_2$, or $-NR^9(CH_2)_2$, and wherein R^8 is Ar^2, or R^8 and R^9, taken together with the nitrogen atom, form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen or sulfur and compounds have one of formulas **II-D or III-D:**

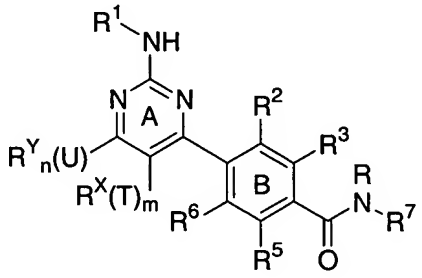


II-D

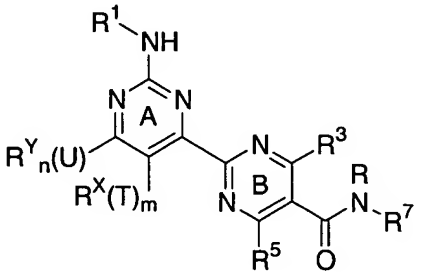


III-D

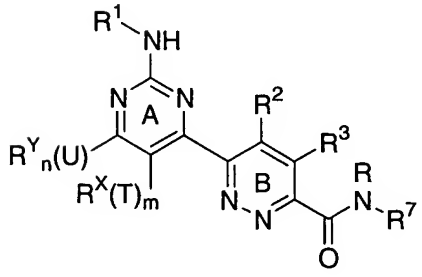
38. The compound of claim 37, wherein for compounds of formula **II-D,** ring B is selected from **i, ii, iii, iv, vi, viii, ix, xii,** or **xiv** and compounds have one of formulas **II-D-i, II-D-ii, II-D-iii, II-D-iv, II-D-vi, II-D-viii, II-D-ix, II-D-xii,** or **II-D-xiv**:



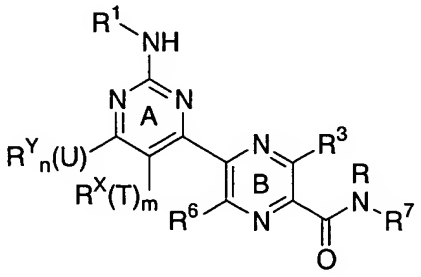
II-D-i



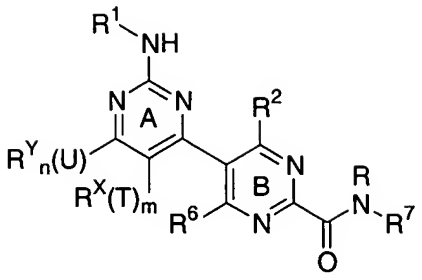
II-D-ii



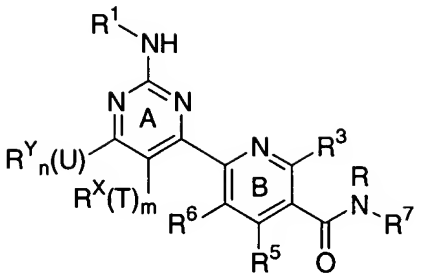
II-D-iii



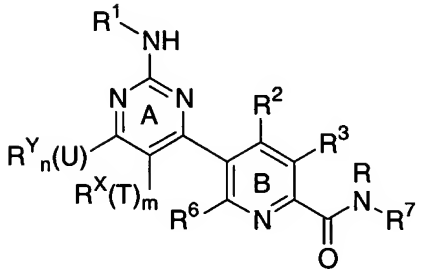
II-D-iv



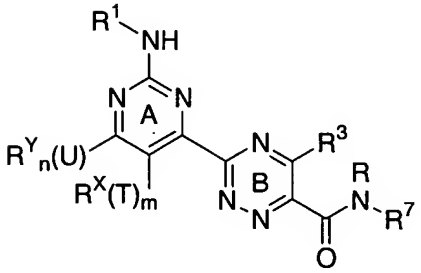
II-D-vi



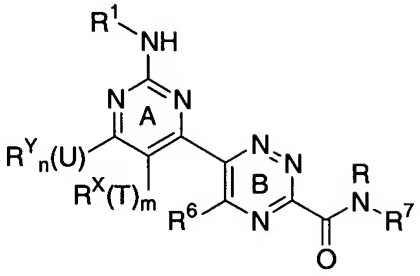
II-D-viii



II-D-ix

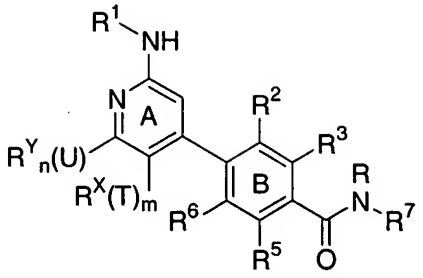


II-D-xii

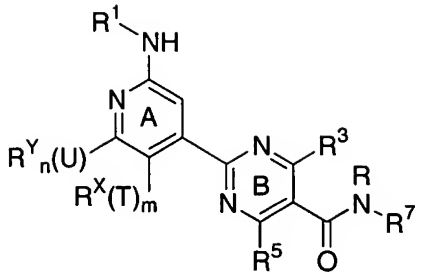


II-D-xiv

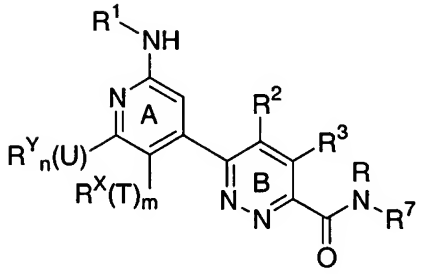
39. The compound of claim 37, wherein for compounds of formula **III-D,** ring B is selected from **i, ii, iii, iv, vi, viii, ix, xii,** or **xiv** and compounds have one of formulas **III-D-i, III-D-ii, III-D-iii, III-D-iv, III-D-vi, III-D-viii, III-D-ix, III-D-xii,** or **III-D-xiv**:



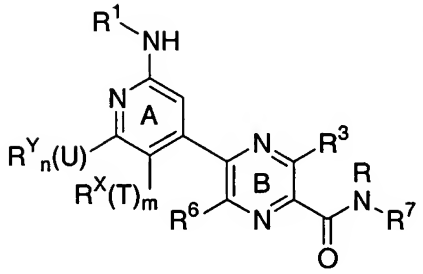
III-D-i



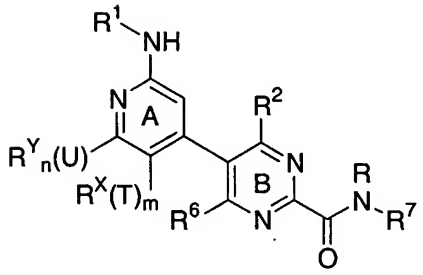
III-D-ii



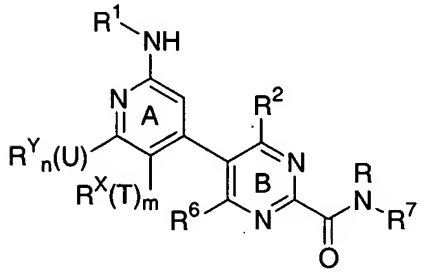
III-D-iii



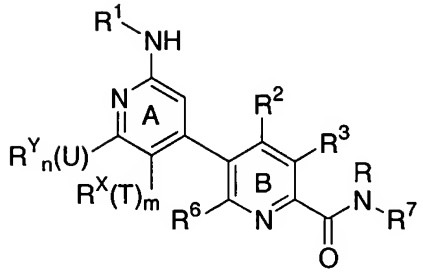
III-D-iv



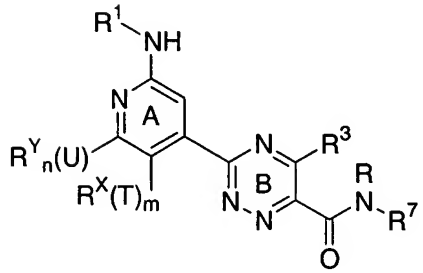
III-D-vi



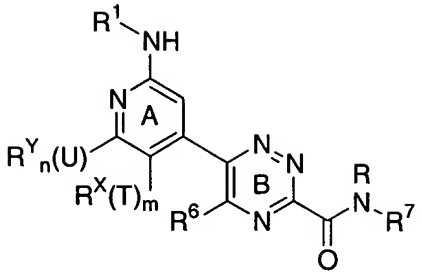
III-D-viii



III-D-ix

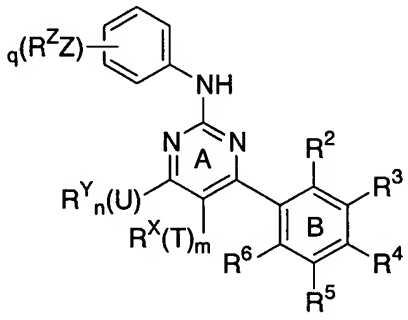


III-D-xii

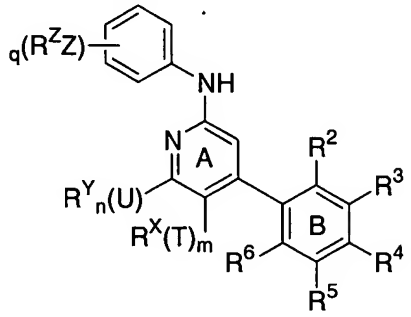


III-D-xiv

40. The compound of claim 1, where R^1 is optionally substituted phenyl and ring B is an optionally substituted phenyl group and compounds have the general formulas **IV** or **V:**

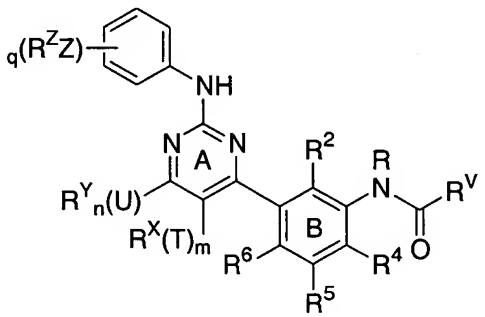


IV

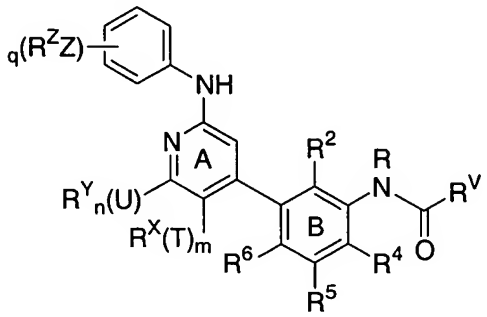


V

41. The compound of claim 40, wherein, R^3 is $NRCOR^7$ and compounds have the general formulae **IV-A-(i)** or **V-A-(i):**

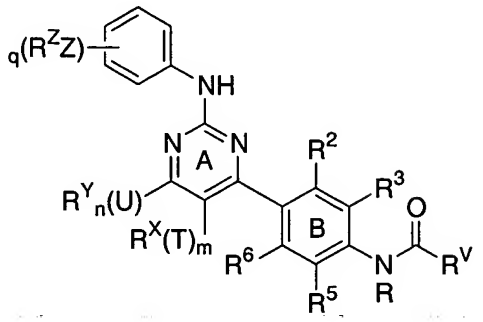


IV-A-(i)

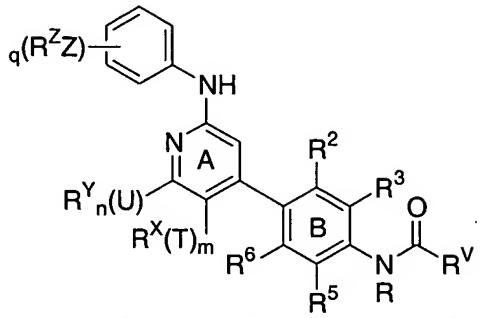


V-A-(i)

42. The compound of claim 40, wherein R^4 is $NRCOR^7$ and compounds have the general formulae **IV-B-(i)** or **V-B-(i):**

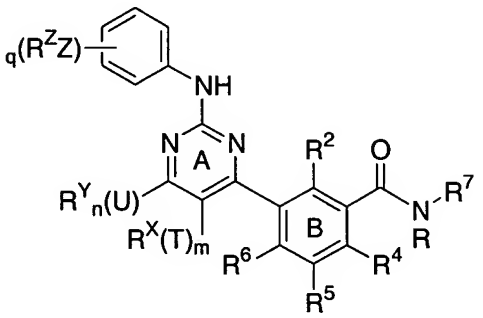


IV-B-(i)

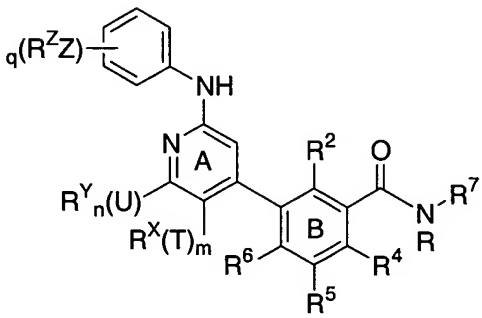


V-B-(i)

43. The compound of claim 40, wherein R^3 is $CONRR^7$ and compounds have the general formulae **IV-C-(i)** or **V-C-(i):**

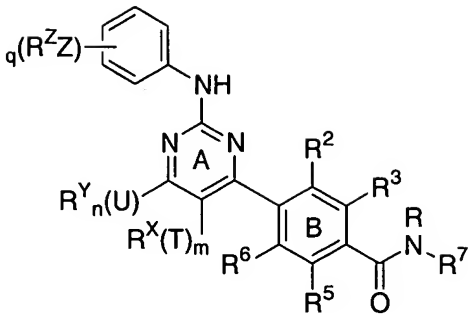


IV-C-(i)

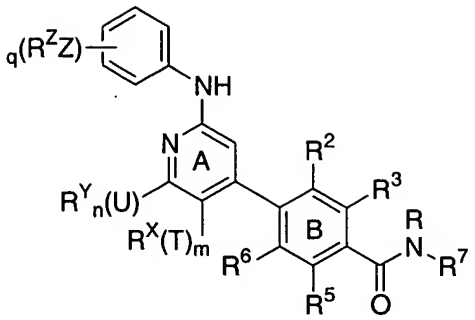


V-C-(i)

44. The compound of claim 40, wherein R^4 is $CONRR^7$ and compounds have the general formulae **IV-D-(i)** or **VII-D-(i):**

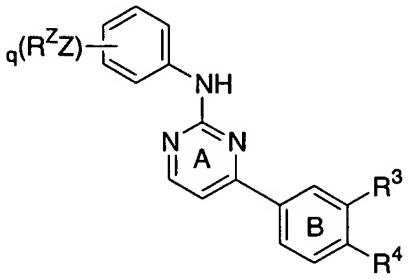


IV-D-(i)

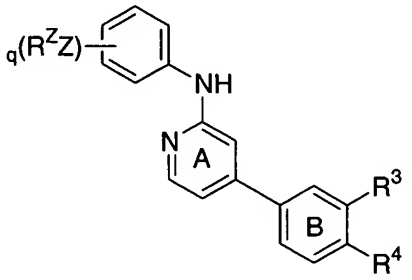


V-D-(i)

45. The compound of claim 40, wherein R^1 is optionally substituted phenyl, ring A is pyrimidinyl or pyridyl, ring B is phenyl, and R^2, R^5, and R^6 are each hydrogen, and compounds have the general formulae **VI** and **VII**:



VI



VII

46. The compound of claim 40 or 45, wherein

a. q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-SO_2NH_2$;

b. R^3 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (**a**), or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r,** and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, -N(R)COR, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

c. R^4 is hydrogen.

47. The compound of claim 40 or 45, wherein:

a. q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-SO_2NH_2$;

b. R^3 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (**a**) or is an optionally substituted heteroaryl moiety selected from one of groups **b** through **r**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR; and

c. R^4 is hydrogen.

48. The compound of claim 40 or 45, wherein:

a. q is 0 or 1 and ZR^Z is -NH_2, -OH, C_{1-4}alkoxy, or -$S(O)_2NH_2$;

b. R^4 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (**a**) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR; and

c. R^3 is hydrogen.

49. The compound of claim 40 or 45, wherein:

a. q is 0 or 1 and ZR^Z is -NH_2, -OH, C_{1-4}alkoxy, or -$S(O)_2NH_2$;

b. R^4 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0, Y is a bond, and R^8 is phenyl (**a**) or an optionally substituted heteroaryl moiety selected from one of groups **b** through **z**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR; and

c. R^3 is hydrogen.

50. The compound of claim 40 or 45, wherein:

a. q is 0 or 1 and ZR^Z is -NH_2, -OH, C_{1-4}alkoxy, or -$S(O)_2NH_2$;

b. R^3 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, -$(R)_2$, -OR, -SR, -$SO_2N(R)_2$, -$N(R)SO_2R$, -N(R)COR, -$N(R)_2$, -CH_2OR, -$CH_2N(R)_2$, or -CH_2SR; and

c. R^4 is hydrogen.

51. The compound of claim 40 or 45, wherein:

a. q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$;

b. R^3 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, -N(R)COR, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

c. R^4 is hydrogen.

52. The compound of claim 40 or 45, wherein:

a. q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$;

b. R^4 is $NRCOR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents include halogen, C_{1-4}alkyl, NH_2, OH, SH, SO_2NH_2, C_{1-4}alkoxy, C_{1-4}thioalkyl, CH_2OR, $CH_2N(R)_2$, or CH_2SR; and

c. R^3 is hydrogen.

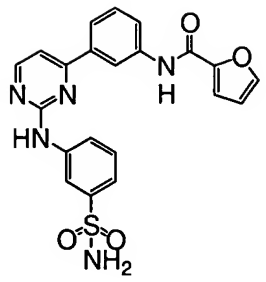
53. The compound of claim 40 or 45, wherein:

a. q is 0 or 1 and ZR^Z is $-NH_2$, -OH, C_{1-4}alkoxy, or $-S(O)_2NH_2$;

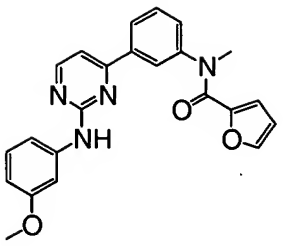
b. R^4 is $CONRR^7$, wherein R^7 is $(CH_2)_t$-Y-R^8, and t is 0 or 1, Y is NR^9, and R^8 and R^9, taken together with the nitrogen atom, form a group selected from **s**, **t**, **u**, or **v**, and wherein r is 0 or 1, and WR^W substituents are halogen, C_{1-4}alkyl, $-(R)_2$, -OR, -SR, $-SO_2N(R)_2$, $-N(R)SO_2R$, -N(R)COR, $-N(R)_2$, $-CH_2OR$, $-CH_2N(R)_2$, or $-CH_2SR$; and

c. R^3 is hydrogen.

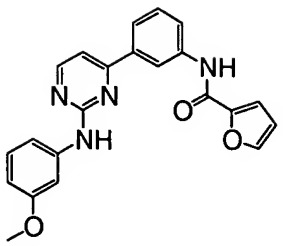
54. The compound of claim 1, having one of the following structures:



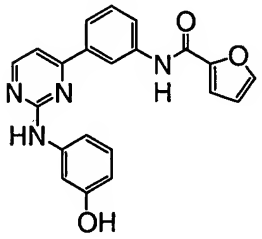
IV-A(i)-1



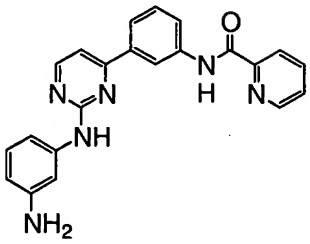
IV-A(i)-2



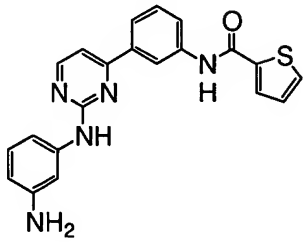
IV-A(i)-3



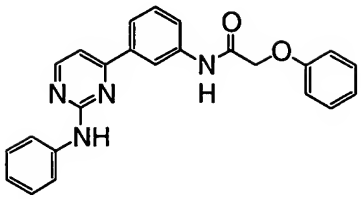
IV-A(i)-4



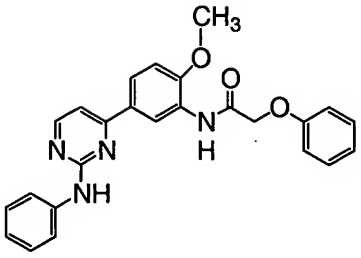
IV-A(i)-5



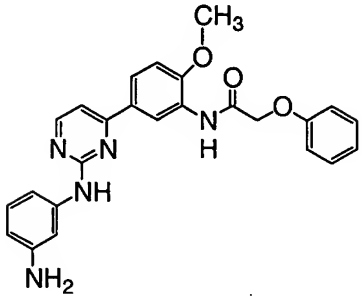
IV-A(i)-6



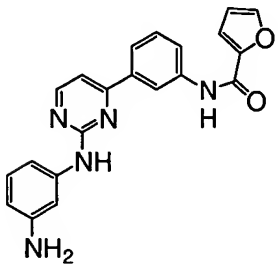
IV-A(i)-7



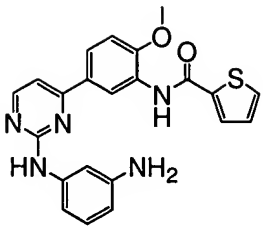
IV-A(i)-8



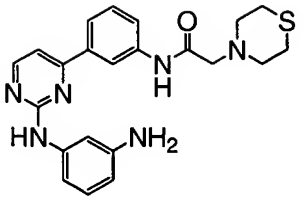
IV-A(i)-9



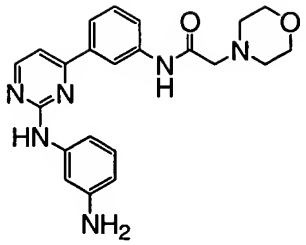
IV-A(i)-10



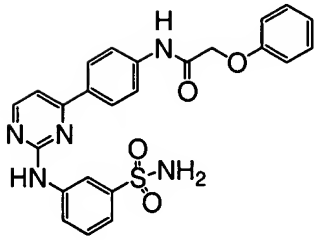
IV-A(i)-11



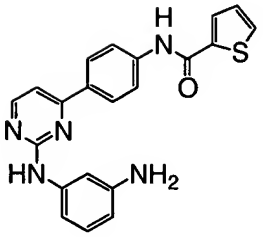
IV-A(i)-12



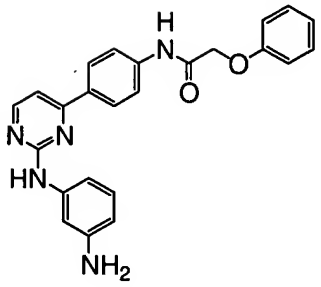
IV-A(i)-13



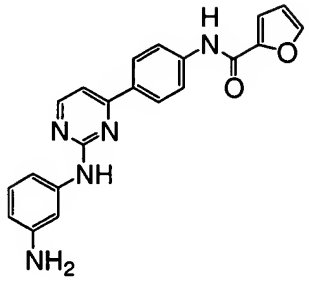
IV-B(i)-1



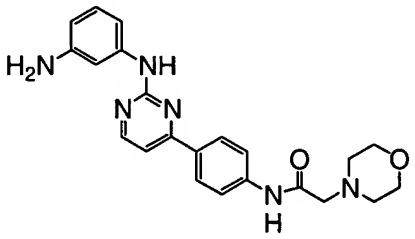
IV-B(i)-2



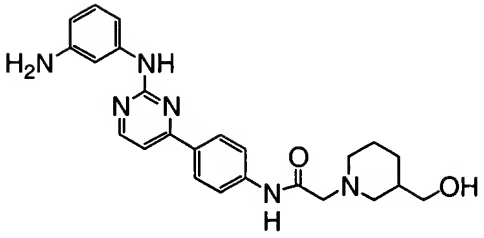
IV-B(i)-3



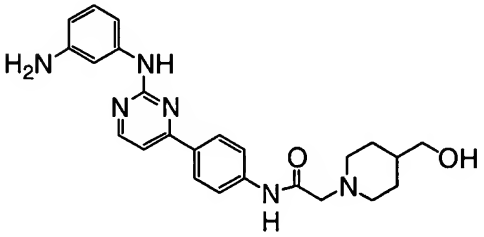
IV-B(i)-4



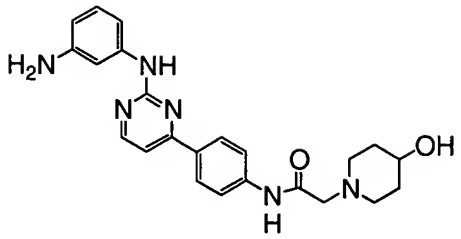
IV-B(i)-5



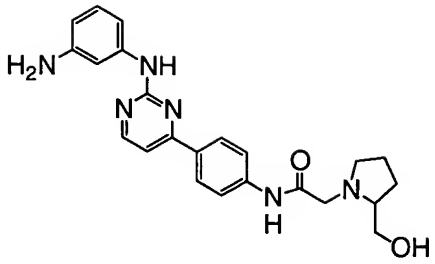
IV-B(i)-6



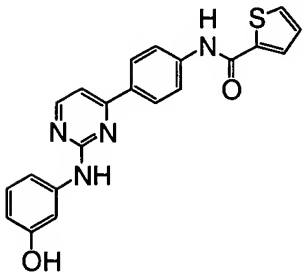
IV-B(i)-7



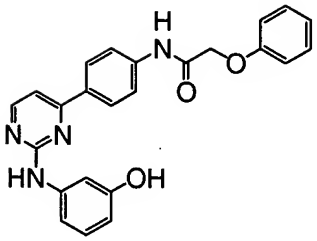
IV-B(i)-8



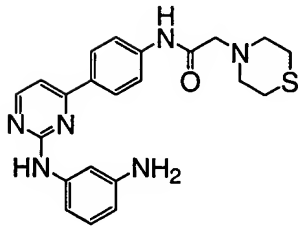
IV-B(i)-9



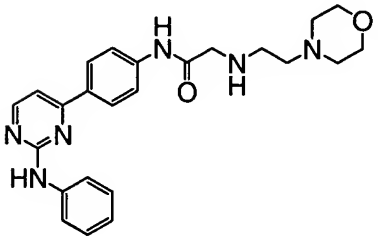
IV-B(i)-10



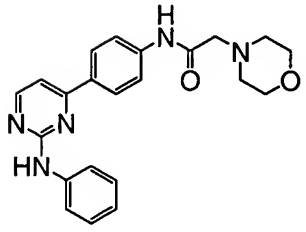
IV-B(i)-11

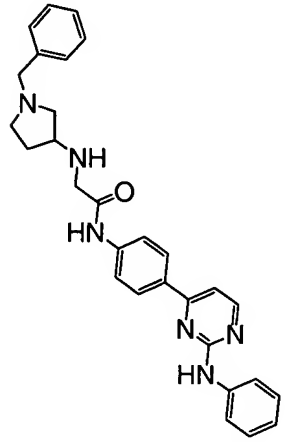


IV-B(i)-12

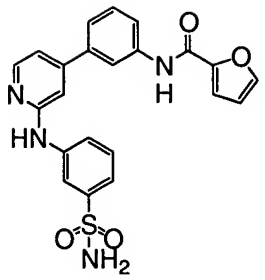


IV-B(i)-13

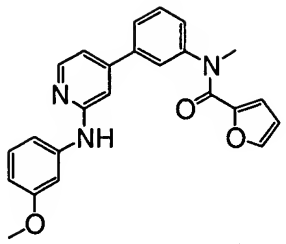


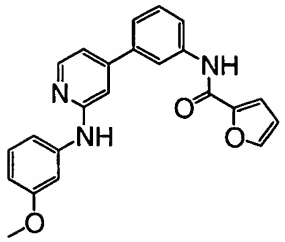


IV-B(i)-14

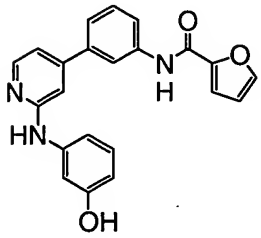


IV-B(i)-15

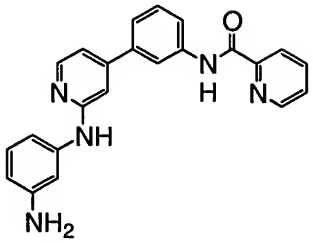




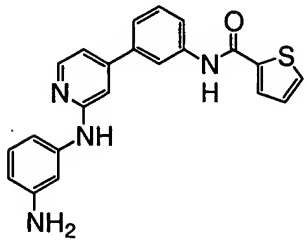
V-A(i)-1



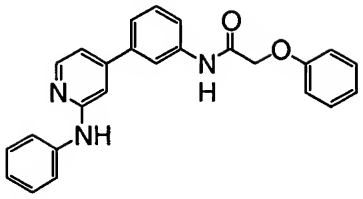
V-A(i)-2



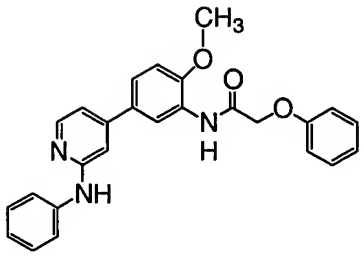
V-A(i)-3



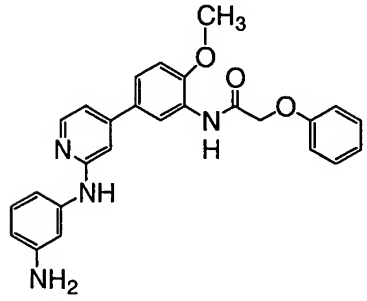
V-A(i)-4



V-A(i)-5

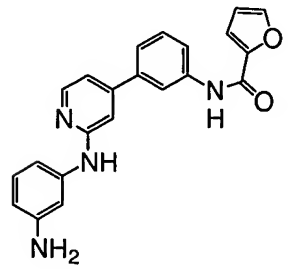


V-A(i)-6

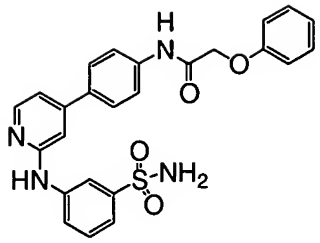


V-A(i)-7

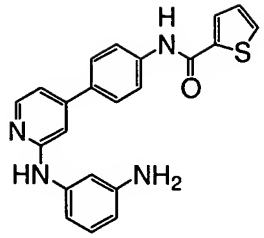
V-A(i)-8

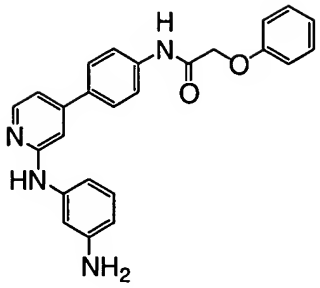


V-A(i)-9



V-A(i)-10

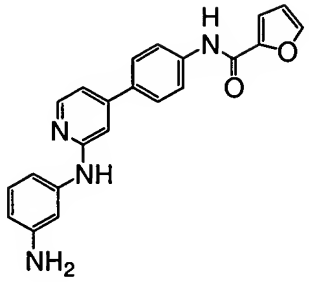


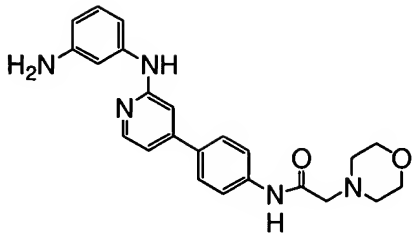


V-B(i)-1

V-B(i)-2

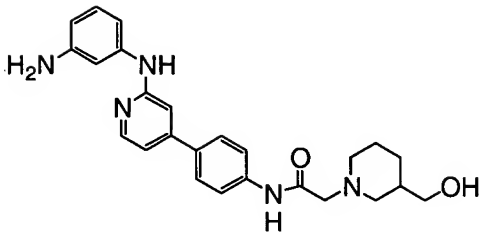
V-B(i)-3

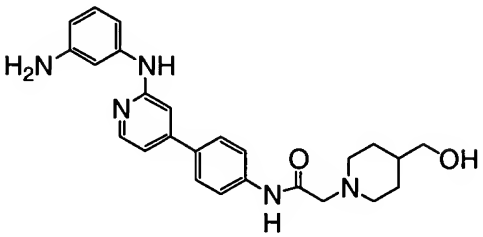




V-B(i)-4

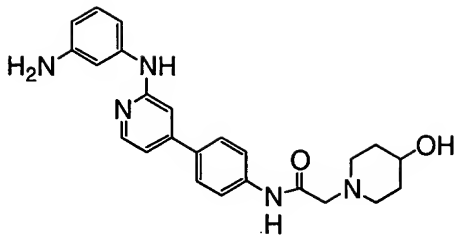
V-B(i)-5



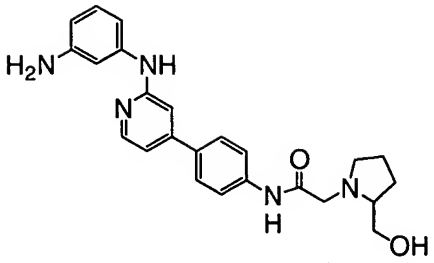


V-B(i)-6

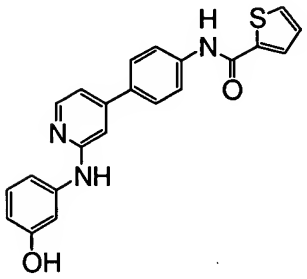
V-B(i)-7



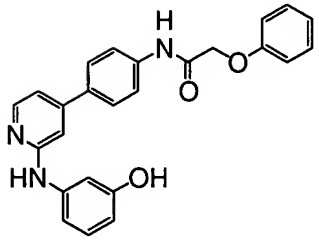
V-B(i)-8



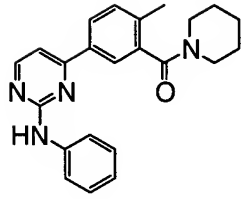
V-B(i)-9



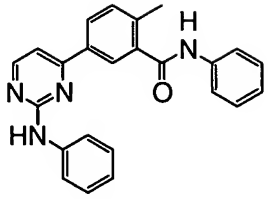
V-B(i)-10



V-B(i)-11



IV-C(i)-1



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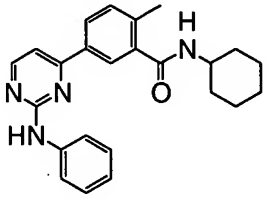

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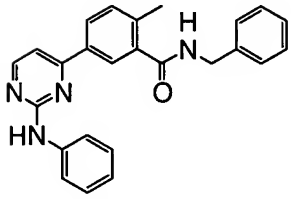

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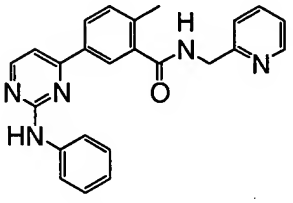

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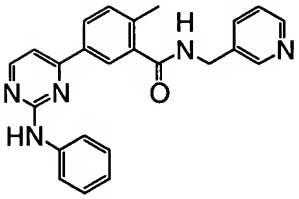
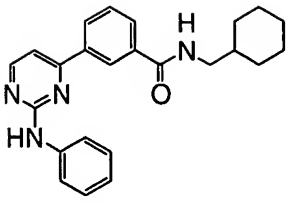
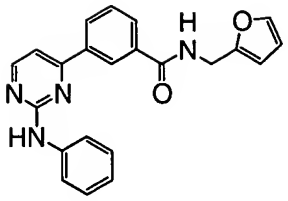


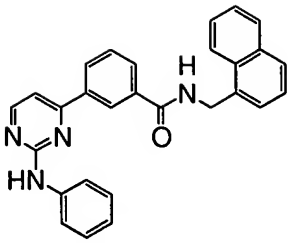
IV-C(i)-6



IV-C(i)-7



IV-C(i)-8



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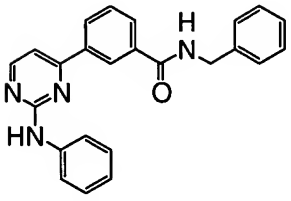

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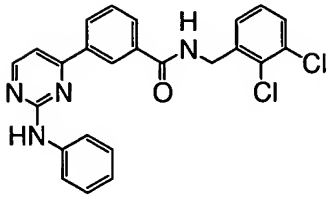

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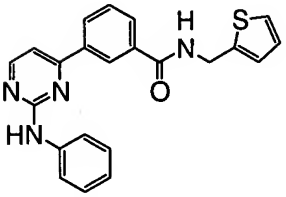

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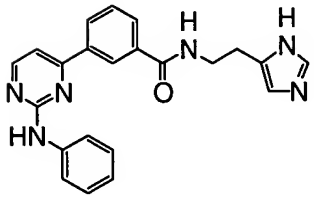
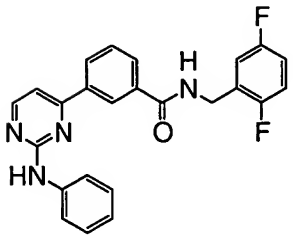
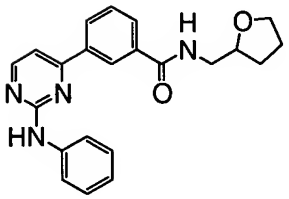


IV-C(i)-13



IV-C(i)-14



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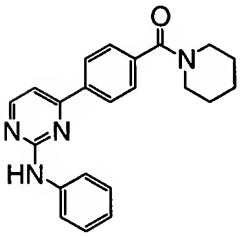
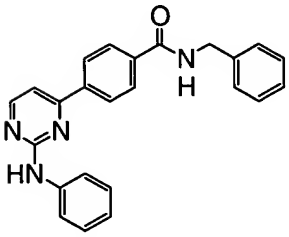


IV-D(i)-1



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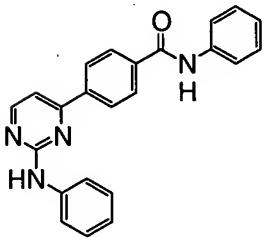

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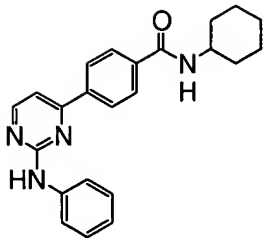
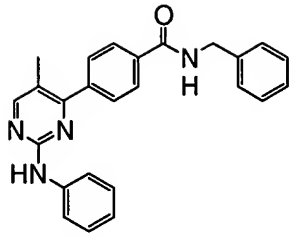


IV-D(i)-4



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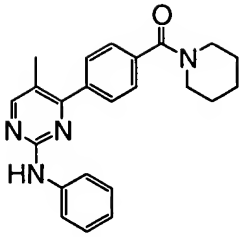
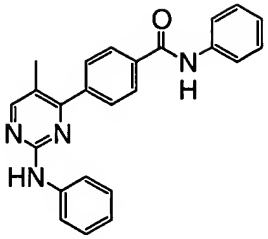
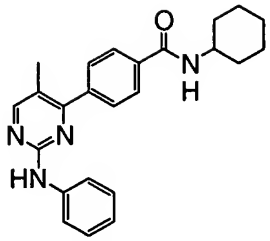


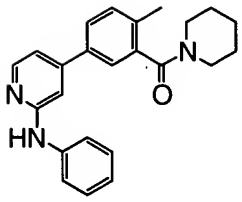
IV-D(i)-6



IV-D(i)-7



IV-D(i)-8



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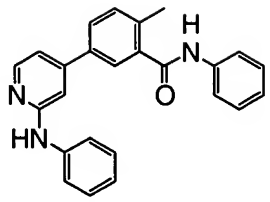

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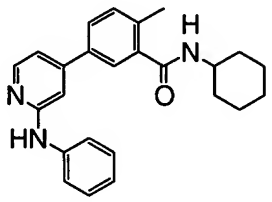

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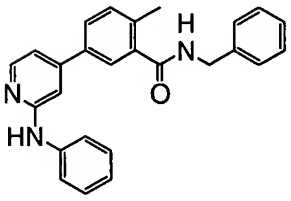

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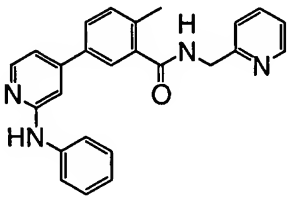

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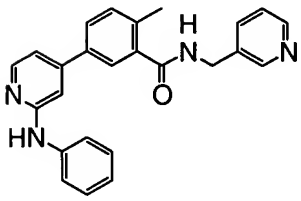
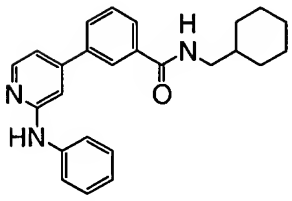
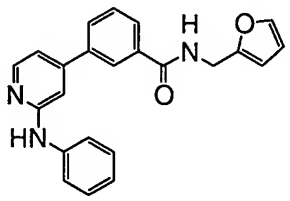
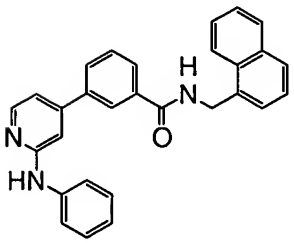


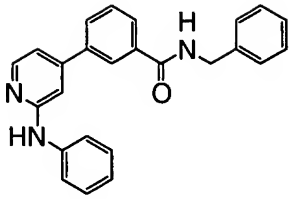
V-C(i)-6



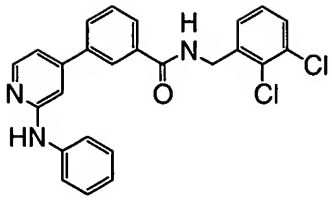




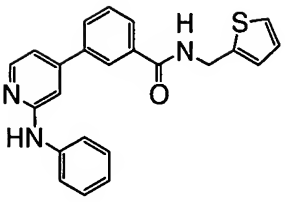
V-C(i)-7



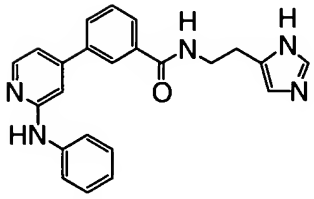
V-C(i)-8



V-C(i)-9



V-C(i)-10



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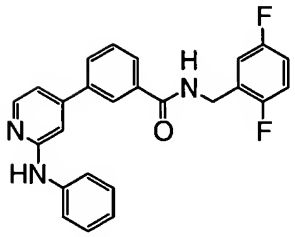
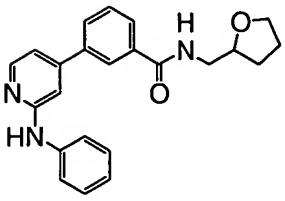
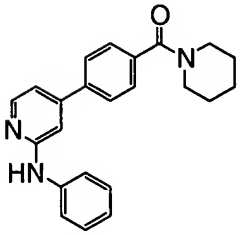


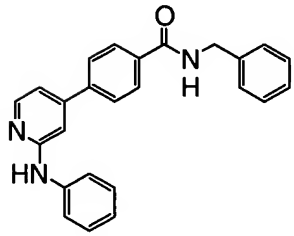
V-C(i)-12



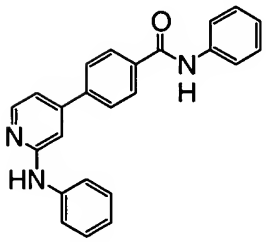
V-C(i)-13



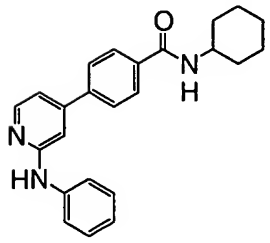
V-C(i)-14



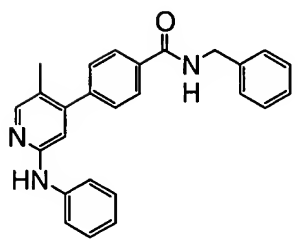
V-C(i)-15



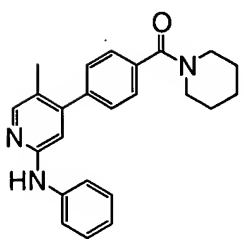
V-D(i)-1



V-D(i)-2



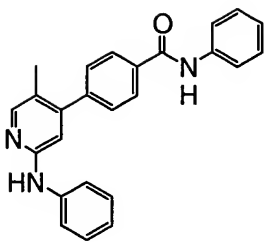
V-D(i)-3



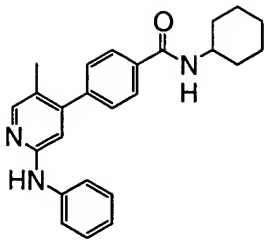
V-D(i)-4

V-D(i)-5

V-D(i)-6



V-D(i)-7



V-D(i)-8

55. A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

56. The composition of claim 55, further comprising an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, a treatment for Alzheimer's Disease, a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder.

57. A method of inhibiting JAK kinase activity in a biological sample or a patient, comprising the step of contacting said biological sample or patient with:

a) the composition of claim 55; or

b) the compound of claim 1.

58. A method of treating or lessening the severity of a disease or disorder selected from an immune response, an autoimmune disease, a neurodegenerative disorder, or a solid or hematologic malignancy comprising administering to a patient in need thereof a compound of claim 1 or a composition of claim 55.

59. The method of claim 58, wherein the disease is an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, rheumatoid arthritis, amyotrophic lateral sclerosis, multiple sclerosis, Familial amyotrophic lateral sclerosis (FALS), leukemia, or lymphoma.